

30-year experience of the Institute of Hematology and Transfusion Medicine, Warsaw, Poland in dry eye syndrome treatment using autologous serum eye drops

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ABSTRACT

BACKGROUND: In 1991, the Institute of Hematology and Transfusion Medicine (IHTM) was the first center in Poland to start the production of serum-based artificial tears, which were applied successfully in the management of multiple etiology dry eye syndrome (DES). DES is a common chronic condition associated with an abnormal tear film secretion, which may cause gritty eyes, eye pain, and often blurred vision.

MATERIAL AND METHODS: The study analysis relied on the data collected over 30 years (1386 autologous whole blood donations from 662 patients), which included: the annual number of donations, patients' age, gender, and underlying disease.

RESULTS: The patient's age at the first visit ranged from 7 to 92 years (55 on average). The vast majority were women (77%). DES of various severity and etiology was identified among the adult patients, and the most common disease entities were graft-versus-host disease (GvHD), Sjögren's syndrome, rheumatoid arthritis, glaucoma, cataracts, and corneal damage due to trauma and/or surgery.

CONCLUSIONS: Many scientific reports confirm the effect of artificial tears in the treatment of DES. In Poland, artificial tears is still an underused therapy due to the high costs generated by expensive disposable materials and equipment and the time-consuming procedure of preparing eye drops for one patient.

KEY WORDS: artificial tears; serum eye drops; autologous serum; dry eye syndrome; DES; GvHD; Sjögren's syndrome

Ophthalmol J 2023; Vol. 8, 56–61

INTRODUCTION

Dry eye syndrome (DES) is a common chronic condition associated with abnormal tear film secretion and is diagnosed as the source cause

of significant discomfort. DES is characterized by a feeling of sand under the eyelids, eye pain, and sometimes blurred vision. The Institute of Hematology and Transfusion Medicine (IHTM)

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was the first center in Poland to start the production of serum-based artificial tears, which were effective for managing multiple etiology DES. The product is recommended particularly for patients unresponsive to standard preservative eye drops and those hitherto unsuccessfully treated for DES. It is worth noting that serum drops contain such substances as transforming growth factor β (TGF- β), epidermal growth factor (EGF), vitamins A and E, and immunoglobulins [1, 2] therefore, serum-based eye drops have a beneficial effect on the eyeball. The study's aim was to present the statistical data for a 30-year period for IHTM patients who applied artificial tears and to demonstrate the growing awareness of both patients and physicians regarding DES therapy with autologous as well as allogeneic tears collected from healthy AB male donors.

MATERIALS AND METHODS

The study analysis was based on the data collected over 30 years from orders for artificial tears issued by ophthalmologists and IHTM physicians (in the case of patients suffering from DES due to GvHD after stem cell transplantation). The data included: age at the first visit, gender, underlying disease, and the number of donations per patient. The study group included 662 patients (508 women and 154 men) who used autologous serum eye drops between 1991 and 2021. The most common indication for applying artificial tears was DES (of various severity and etiology). Most IHTM patients

appeared only once (444). The persons referred to IHTM for preparation of artificial tears were usually unresponsive to treatment with conventional methods — eye lubricating medicinal products. The procedure for artificial tears preparation is presented in the following section.

We also performed a statistical analysis of data covering the annual number of artificial tear products considering the impact of the COVID-19 pandemic.

Autologous artificial tears preparation

Serum eye drops were prepared under sterile conditions in a laminar airflow chamber. After finding the patient eligible for the procedure, 150–450 mL of whole blood (WB) was collected into a bag with no anticoagulant. The bag was left to rest in an incubator for a maximum of 2 hours at 37°C. The coagulated blood was then centrifuged to obtain serum. When artificial tears were first prepared, the centrifugation was performed only once. Because of the risk that any cellular elements may have remained in serum, the coagulated blood is currently subjected to two centrifugations. Empty containers for serum transfer were sterile-connected within a closed system. Following the second centrifugation, the serum was transferred into disposable sterile-packed 1.5 mL tubes in a laminar chamber. Finally, with a heat sealer, the tubes were divided into capsules of approximately 1 cm length (Fig. 1). The capsules were then frozen within 18 hours of blood collection. The sterile environment and special equip-

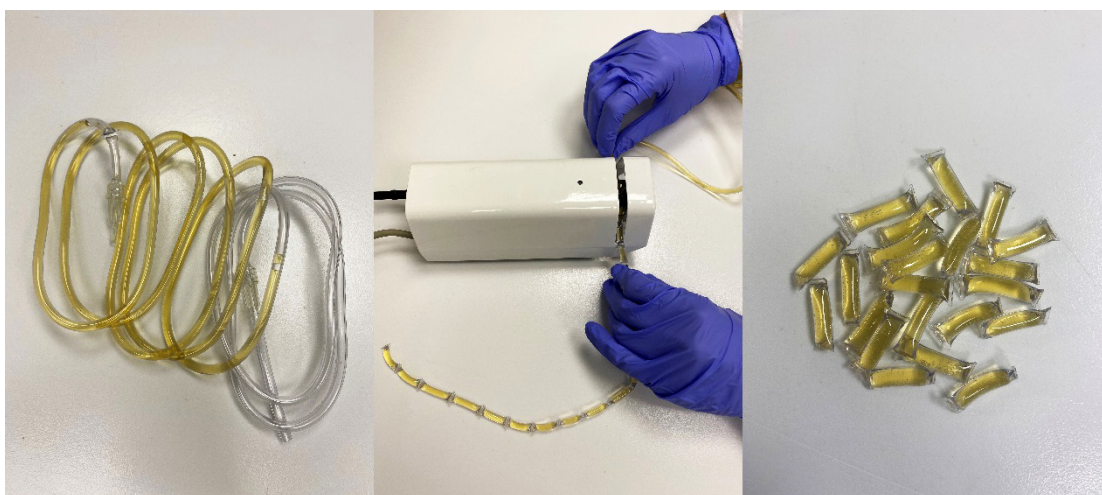


FIGURE 1. Final preparation step, tubes are divided into the app. 1 cm capsules

ment used during preparation were the safeguards of the quality of the serum eye drops. Appropriate storage conditions were provided (temperature $< -20^{\circ}$) [3].

Typically, artificial tears are used 1–5 times daily, 1 drop per eye, according to the patient's needs and the ophthalmologist's recommendations. Patients often reduce the dosage after feeling improvement. Capsules should be defrosted immediately before application.

The patient must be adequately prepared for blood collection to obtain a high-quality product. The patient should appear for the procedure after a light breakfast, and any anticoagulant medication must be discontinued (if possible) several days before blood collection [4]. An average of 400 to 700 capsules are prepared from a single 150 ml donation of WB. The volume of the serum depends on the patient's health, age, and underlying disease.

RESULTS

IHTM statistics

Over the last 30 years, the number of patients reporting at IHTM for autologous artificial tears has been growing steadily. Figure 2 presents the number of artificial tears prepared annually. Over the last five years, these numbers have markedly increased,

exceeding 100 patients per year. Since 2016, paediatric artificial tears production has been launched in cooperation with Children's Clinical Hospital in Warsaw. At IHTM, 17 children (a total of 23 donations) have benefited from eye drops.

The COVID-19 pandemic markedly reduced the number of artificial tears products prepared in the first half of 2020. In 2019, an average of 12 products were prepared monthly, while between March and May 2020, the number dropped to 3 (the annual average for 2020 was 9). The pandemic restrictions had a significant impact on the procedure of autologous product preparation. The conditions had to be extra safe. Therefore, during the pandemic and lockdown period, the IHTM offered patients allogenic artificial tears prepared from fully screened blood donors. The drops were available, and there was no need to collect autologous WB. The patient picked up the drops during a short visit to the hospital and was thus less exposed to contact with other people.

Age and gender of patients

During the period under review, 662 patients were referred to IHTM for autologous eye drops. Their age and gender varied. At the first visit, the age ranged from 7 to 92 years (55 on average). The patients were divided into five age groups: below 18 years (paediatric patients), 18–30 years, 30–55 years, 55–70 years, and over 70 years (Fig. 3).

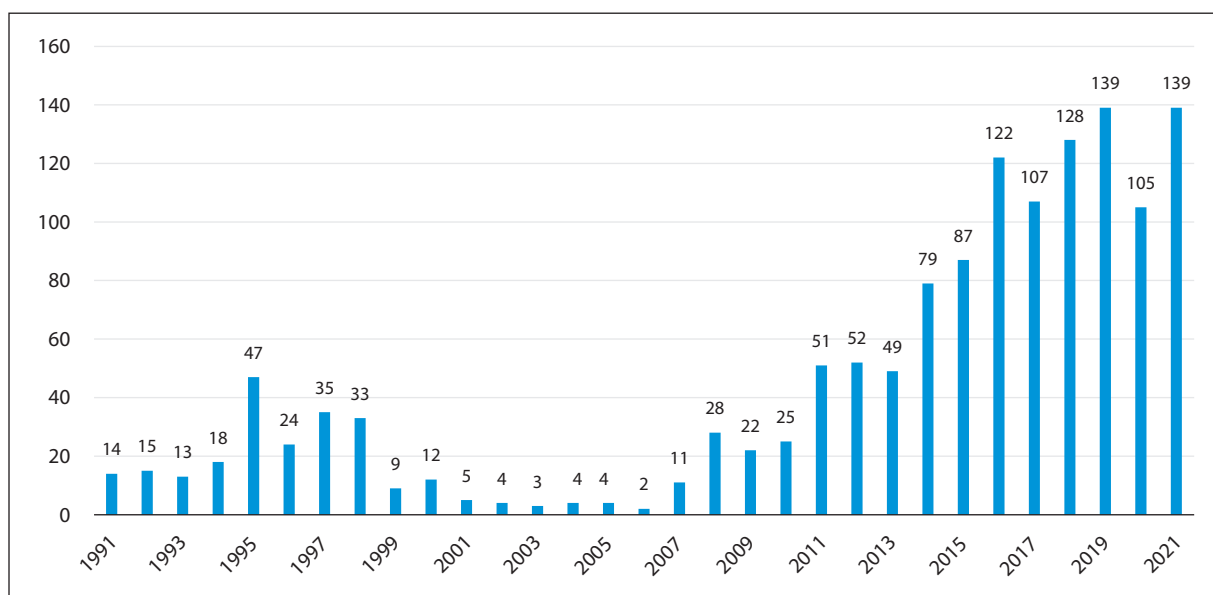


FIGURE 2. Patients reporting for preparation of artificial tears at Institute of Hematology and Transfusion Medicine, Warsaw (IHTM) in the period 1991–2021

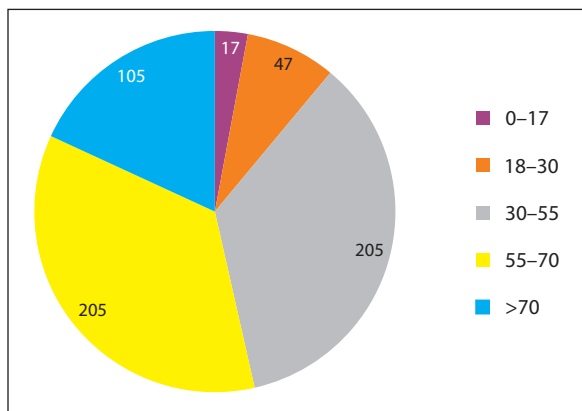


FIGURE 3. Age of patients at the first visit to Institute of Hematology and Transfusion Medicine, Warsaw (IHTM) for autologous artificial tears

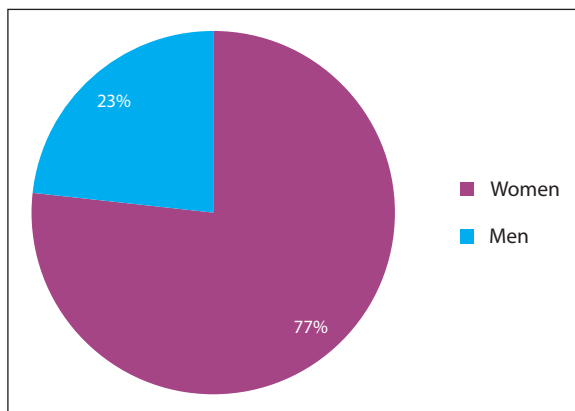


FIGURE 4. Gender of patients using autologous artificial tears at Institute of Hematology and Transfusion Medicine, Warsaw (IHTM) between 1991 and 2021

The largest age groups to start treatment with artificial tear were 30–55 years (205 patients, 35%) and 55–70 years (205 patients, 35%). The vast majority were women, 77% (Fig. 4).

Over the last 30 years, a total of 1386 donations were collected for the purpose of preparing autologous serum eye drops. Patients usually appeared at IHTM for a single WB donation to have artificial tears prepared for them (67%). The highest number of donations per patient was 65. This female patient (now 67) suffered from chronic DES caused by corneal damage with eyelid regurgitation. This patient has been using drops since 1992.

Disease entities

On 292 orders which referred patients to IHTM for preparation of autologous artificial tears, the underlying disease was clearly specified. Several disease entities were identified, such as DES of various severity and etiology — autoimmune diseases like Sjögren’s syndrome, often secondary to rheumatoid arthritis (RA), DES in the course of glaucoma or cataracts, lacrimal gland or corneal damage due to trauma and/or surgery, chronic keratoconjunctivitis or conjunctivitis, and some congenital diseases, including achromatopsia. We identified single cases of Fuchs’ dystrophy, Lyell’s syndrome, aplastic anaemia, scarring pemphigoid, or neurological conditions. The indications for the use of artificial tears are summarised in Table 1.

Some patients who reported to IHTM only once suffered from other conditions such as degenerative myopia, fibromyalgia, juvenile arthritis, atopic corneal inflammation, ulceration, erosion, chemical burn, and post-surgery condition.

Disease entity	% of patients
Dry eye syndrome of various severity	45%
GvHD	23%
Sjögren’s syndrome	17%
Dry eye syndrome secondary to rheumatoid arthritis	3%
Keratitis	2%
Glaucoma	2%
Trauma/surgery-related eye damage	2%
Keratopathy	1%
Other	3%

GvHD — graft versus host disease

DISCUSSION

Worldwide, artificial tears are applied in managing many ocular diseases. Non-preservative serum eye drops are particularly beneficial for patients allergic to the components of medicinal eye drops [5, 6]. Nowadays, serum is commonly used for the treatment of DES, and the results are promising. The number of patients who use artificial tears is growing annually. Such patients report less pain and burning sensation, less tearing and redness, no headaches as well as reduced hypersensitivity to light. The positive effects of artificial tears also include a return to activities that were precluded because of DES (extended reading, TV watching, using the mobile phone and cash machine, or driving). Ophthalmologists also confirm the improvement of the eye condition. After several years of regular use of serum drops, patients report significant quality

of life improvement compared to their experience with medicinal eye drops. We were unable to determine why one time-patients failed to appear for the subsequent visits — either artificial tears were so effective that the therapy was discontinued or exactly the opposite. Relying on literature reports and opinions of IHTM patients who use artificial tears merely to control inflammation or before surgery (corneal disease), we may, however, assume that even a single application of the drops gives satisfactory results and further application of serum eye drops may not be required.

Analysis of global data for the use of artificial tears has demonstrated a wide variety of patient-related characteristics. Women were much more likely to use the product, which, among others, is related to their higher susceptibility to autoimmune diseases, which may underly DES [7]. Several studies confirm DES to be more common in middle-aged and elderly patients [8–11]. Most commonly described in the literature is using artificial tears to manage conditions such as Sjögren's syndrome, GvHD in haematological patients following allogeneic haematopoietic stem cell transplantation, or corneal disorders, also after surgery [12–15]. In our group of patients, the diseases mentioned above were the most common indications for the use of artificial tears.

For several decades now, artificial tears have been used worldwide to manage DES effectively. The widespread use of serum drops was pioneered in the 1970s by Ralph et al. [16]. There were, however, no uniform preparation standards either at the European or national level. Hence, each facility prepared the product according to in-house procedures. This refers to autologous and allogeneic artificial tears [4, 11, 17]. In some centres, 20% or 50% dilutions, e.g., with saline or sodium hyaluronate, are used for dry eye treatment in the course of autoimmune diseases [18]. The patients evaluated at IHTM applied undiluted eye drops from 100% autologous serum.

IHTM was the first facility in Poland to prepare artificial tears. Since the 1990s, procedures have been elaborated to ensure maximum product safety. IHTM has launched training courses on artificial tears preparation to popularise serum eye drops. The courses are dedicated to the personnel of Polish blood transfusion centres. As a result, many of the centers have implemented procedures for autologous eye drop preparation. Currently, patients countrywide have easier access to the prod-

uct prepared in several Regional Blood Transfusion Centres.

Autologous serum drops should only be prepared at facilities dealing with blood and blood components or at cell banks. They provide a sterile environment and special equipment indispensable for the preparation of the high-quality, safe product.

In 2018, the motivation to increase the patients' access to serum eye drops led to the initiation at IHTM the production of artificial tears prepared from allogeneic serum. Allogeneic artificial tears are usually used in DES treatment for patients with problems at blood collection (advanced age or chemotherapy) or on anticoagulants that cannot be discontinued. By the end of 2021, 70 patients had benefited from allogeneic artificial tears prepared at IHTM. Allogeneic drops were also available during the first months of the COVID-19 pandemic when autologous donations were temporarily stopped.

CONCLUSIONS

Many scientific reports confirm the effect of artificial tears in the treatment of DES. In Poland, artificial tears are still an underused therapy due to high costs (500–700 PLN for approximately 500 individual capsules) related to expensive disposable materials and equipment and the time-consuming procedure of preparing eye drops for individual patients. In most diseases that underly DES (Sjögren's syndrome or corneal diseases), such drops are not used because of the lack of reimbursement from public funding.

Funding

None declared.

Conflict of interest

The authors declare no conflict of interest.

REFERENCES

1. Gupta A, Monroy D, Ji Z, et al. Transforming growth factor beta-1 and beta-2 in human tear fluid. *Curr Eye Res.* 1996; 15(6): 605–614. doi: [10.3109/02713689609008900](https://doi.org/10.3109/02713689609008900), indexed in Pubmed: [8670763](https://pubmed.ncbi.nlm.nih.gov/8670763/).
2. Soni NG, Jeng BH. Blood-derived topical therapy for ocular surface diseases. *Br J Ophthalmol.* 2016; 100(1): 22–27, doi: [10.1136/bjophthalmol-2015-306842](https://doi.org/10.1136/bjophthalmol-2015-306842), indexed in Pubmed: [26178904](https://pubmed.ncbi.nlm.nih.gov/26178904/).
3. Guide to the Quality and Safety of Tissues and Cells for Human Application. 4th Edition. European Directorate for the Quality of Medicines & HealthCare of the Council of Europe (EDQM); 2019.
4. Antoniewicz-Papis J. Artificial tears to treat dry eye syndrome. *Acta Haematologica Polonica.* 2021; 52(4): 412–415, doi: [10.5603/ahp.2021.0077](https://doi.org/10.5603/ahp.2021.0077).
5. Drew VJ, Tseng CL, Seghatchian J, et al. Reflections on Dry Eye Syndrome Treatment: Therapeutic Role of Blood Products. *Front*

- Med (Lausanne). 2018; 5: 33, doi: [10.3389/fmed.2018.00033](https://doi.org/10.3389/fmed.2018.00033), indexed in Pubmed: [29527528](https://pubmed.ncbi.nlm.nih.gov/29527528/).
6. Fox RI, Chan R, Michelson JB, et al. Beneficial effect of artificial tears made with autologous serum in patients with keratoconjunctivitis sicca. *Arthritis Rheum.* 1984; 27(4): 459–461, doi: [10.1002/art.1780270415](https://doi.org/10.1002/art.1780270415), indexed in Pubmed: [6712760](https://pubmed.ncbi.nlm.nih.gov/6712760/).
 7. Matossian C, McDonald M, Donaldson KE, et al. Dry Eye Disease: Consideration for Women's Health. *J Womens Health (Larchmt).* 2019; 28(4): 502–514, doi: [10.1089/jwh.2018.7041](https://doi.org/10.1089/jwh.2018.7041), indexed in Pubmed: [30694724](https://pubmed.ncbi.nlm.nih.gov/30694724/).
 8. Vehof J, Snieder H, Jansonius N, et al. Prevalence and risk factors of dry eye in 79,866 participants of the population-based Lifelines cohort study in the Netherlands. *Ocul Surf.* 2021; 19: 83–93, doi: [10.1016/j.jtos.2020.04.005](https://doi.org/10.1016/j.jtos.2020.04.005), indexed in Pubmed: [32376389](https://pubmed.ncbi.nlm.nih.gov/32376389/).
 9. Baer AN, Walitt B. Update on Sjögren Syndrome and Other Causes of Sicca in Older Adults. *Rheum Dis Clin North Am.* 2018; 44(3): 419–436, doi: [10.1016/j.rdc.2018.03.002](https://doi.org/10.1016/j.rdc.2018.03.002), indexed in Pubmed: [30001784](https://pubmed.ncbi.nlm.nih.gov/30001784/).
 10. Clayton JA, Clayton JA. Dry Eye. *N Engl J Med.* 2018; 378(23): 2212–2223, doi: [10.1056/NEJMra1407936](https://doi.org/10.1056/NEJMra1407936), indexed in Pubmed: [29874529](https://pubmed.ncbi.nlm.nih.gov/29874529/).
 11. Pan Q, Angelina A, Marrone M, et al. Autologous serum eye drops for dry eye. *Cochrane Database Syst Rev.* 2013; 8(8): CD009327, doi: [10.1002/14651858.CD009327.pub2](https://doi.org/10.1002/14651858.CD009327.pub2), indexed in Pubmed: [23982997](https://pubmed.ncbi.nlm.nih.gov/23982997/).
 12. Kojima T, Dogru M, Kawashima M, et al. Advances in the diagnosis and treatment of dry eye. *Prog Retin Eye Res.* 2020 [Epub ahead of print]: 100842, doi: [10.1016/j.preteyeres.2020.100842](https://doi.org/10.1016/j.preteyeres.2020.100842), indexed in Pubmed: [32004729](https://pubmed.ncbi.nlm.nih.gov/32004729/).
 13. Lekhanont K, Jongkhajornpong P, Anothaisintawee T, et al. Undiluted Serum Eye Drops for the Treatment of Persistent Corneal Epithelial Defects. *Sci Rep.* 2016; 6: 38143, doi: [10.1038/srep38143](https://doi.org/10.1038/srep38143), indexed in Pubmed: [27909310](https://pubmed.ncbi.nlm.nih.gov/27909310/).
 14. Lekhanont K, Jongkhajornpong P, Choubtum L, et al. Topical 100% serum eye drops for treating corneal epithelial defect after ocular surgery. *Biomed Res Int.* 2013; 2013: 521315, doi: [10.1155/2013/521315](https://doi.org/10.1155/2013/521315), indexed in Pubmed: [23984378](https://pubmed.ncbi.nlm.nih.gov/23984378/).
 15. Tahmaz V, Gehlsen U, Sauerbier L, et al. Treatment of severe chronic ocular graft-versus-host disease using 100% autologous serum eye drops from a sealed manufacturing system: a retrospective cohort study. *Br J Ophthalmol.* 2017; 101(3): 322–326, doi: [10.1136/bjophthalmol-2015-307666](https://doi.org/10.1136/bjophthalmol-2015-307666), indexed in Pubmed: [27267447](https://pubmed.ncbi.nlm.nih.gov/27267447/).
 16. Ralph RA, Doane MG, Dohlman CH. Clinical experience with a mobile ocular perfusion pump. *Arch Ophthalmol.* 1975; 93(10): 1039–1043, doi: [10.1001/archophth.1975.01010020815015](https://doi.org/10.1001/archophth.1975.01010020815015), indexed in Pubmed: [1180750](https://pubmed.ncbi.nlm.nih.gov/1180750/).
 17. Seghatchian J, van der Meer PF. A concise overview of advances in therapeutic efficacy of serum eye drops and their alternatives to treat dry eye syndrome: Verifying the narratives of clinical consistency beyond the periphery of international inconsistency on the methods of collection and application. *Transfus Apher Sci.* 2015; 53(1): 85–87, doi: [10.1016/j.transci.2015.05.013](https://doi.org/10.1016/j.transci.2015.05.013), indexed in Pubmed: [26143344](https://pubmed.ncbi.nlm.nih.gov/26143344/).
 18. Shtein RM, Shen JF, Kuo AN, et al. Autologous Serum-Based Eye Drops for Treatment of Ocular Surface Disease: A Report by the American Academy of Ophthalmology. *Ophthalmology.* 2020; 127(1): 128–133, doi: [10.1016/j.ophtha.2019.08.018](https://doi.org/10.1016/j.ophtha.2019.08.018), indexed in Pubmed: [31561880](https://pubmed.ncbi.nlm.nih.gov/31561880/).